September 6, 2002 the Examiner has indicated that two issues remain. Applicants believe the present Amendment and Response addresses those remaining objections and places that application in condition for allowance.

Double Patenting

Claims 4-29 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of co-pending US Patent Application Nos. 09/913,075 and 10/023,059. Applicants submit herewith a Terminal Disclaimer by the common Assignee of the present application, US application 09/913,075, and US application 10/023,059, and authorize the necessary fee under 37 CFR § 120(d) of $110 be charge to our deposit account no. 50-0423. Accordingly, applicants respectfully request the withdrawal of this rejection.

Rejections under 35 USC § 112

Claims 4-29 stand rejected under 35 USC § 112, first paragraph for lack of an enabling description. Applicants respectfully traverse, however to expedite the prosecution of the present application applicants have canceled all the method of use claims.

Claims 4, 5 and 14-26 remain in the application and are directed to compositions comprising novel derivatives of felbamate (2-phenyl-1,3-propanediol dicarbamate). Felbamate is FDA approved for the treatment of several forms of epilepsy, however its use is associated with adverse reactions. As described in Example 1, and the specification of the present application, the adverse reactions associated with the administration of felbamate are due to the formation of toxic metabolites (e.g. 2-phenylpropenol, **5**). As shown in Scheme II on page 7 of the application, the felbamate derivatives of the present invention block the formation of toxic metabolites that are produced by administration of felbamate. Furthermore, as demonstrated in standard tests conducted by the National Institute of Neurological Disorders and Stroke, the felbamate derivatives of the present invention possess anti-seizure activity. Thus the novel felbamate derivatives of the present invention retain bioactive properties of the parent compound

but are blocked from forming the toxic metabolites that are produced upon administration of felbamate. Accordingly, applicants respectfully submit that the improved therapeutic compounds and compositions of the present invention fully comply with the requirements of 35 USC § 112, first paragraph.

First of all applicants note the Examiner's conclusion stated in the first Office Action, that "[t]here is no teaching or indication of any kind to motivate anybody for arriving at the instantly claimed structure." Thus the compounds are novel and non-obvious. Secondly, it is well established law that both the utility requirement of 35 USC § 101 and the enablement requirement of 35 USC § 112, first paragraph are satisfied by evidence of *in vitro* bioactivity, in the case of novel compounds. M.P.E.P. §2107; Nelson v. Bowler 626 F.2d 853 (CCPA 1980); M.P.E.P. §2164.02; Cross v. Iizuka 753 F.2d 1040 (Fed Cir 1985). Correlation between *in vitro* animal testing and human pathology is only required for method of treatment claims. Accordingly, applicants respectfully submit the analysis for the enablement of the composition claims should be separate from the analysis of the method of use claims.

Applicants have demonstrated in Examples 3 and 4 that the claimed novel compounds have bioactivity as evidenced by the results obtained from standard convulsant testing and toxicity screening conducted by the National Institute of Neurological Disorders and Stroke. In particular, the results, as presented in Tables 1-6, demonstrate that the claimed compounds possess anti-seizure activity and do not exhibit toxicity at therapeutically relevant doses. Applicants respectfully submit this data provides an adequate disclosure for making and using the claimed compounds in accordance with 35 USC § 112, first paragraph.

The Examiner bears the burden of establishing a reasonable basis to question the enablement provided in the specification and the examples of the application. While the Examiner has cited two additional references that relate to the efficacy of antiepileptic drugs and a method for mathematically determining the biological activity of carbamate analogues, respectively, applicants respectfully submit these references do not cast any doubt on the enablement of the present invention. In particular, the Shields et al article simply states that **pediatric** disorders are notoriously unresponsive to currently available antiepileptic drugs and

that current animal screening methods may not be appropriate for identifying compounds suitable for pediatric applications. However, the present invention is not specifically directed to the treatment of pediatric disorders. Even if it is argued that the claims read on pediatric treatments, it is not the function of a claim to exclude possible inoperative embodiments (Atlas Powder Co. v. E.I. du Pont de Nemours & Co., 750 F.2d 1569 (Fed. Cir. 1984). There is no reason to think the compounds cannot be used to treat adults. Further, as noted in Cross v. Iizuka 753 F.2d 1040 (Fed Cir 1985) knowledge of the pharmacological activities of compounds is beneficial to the medical profession, and requiring more would delay and frustrate researchers by failing to provide an incentive for early public disclosure of such compounds, thereby failing to further the public interest.

Applicants respectfully submit that the pharmacological activity demonstrated in Examples 3 and 4 enables a substantial use of the claimed novel compounds, and such evidence of *in vitro* bioactivity, for a claimed novel compound is sufficient for meeting the requirements of 35 USC § 112, first paragraph. Accordingly, applicants request the withdrawal of the rejection of claims 4, 5 and 14-26.

Method of Use Claims 6-13 and 27-29

Claims 6-13 and 27-29 stand rejected under 35 USC § 112, first paragraph for lack of an enabling description. More particularly, the Examiner contends that applicants have failed to provide an adequate teaching for treating the broad range of diseases embraced by the claims. Applicants contend that given the extensive prior knowledge regarding the parent felbamate compound and the similar structure and reactivity of the present derivatives relative to the parent compound, there is no reason to doubt applicants' assertion that the modified compounds will exhibit the full range of activities that have been previously demonstrated for the parent compound. However, to expedite the prosecution of the application, applicants have canceled claims 6-13 and 27-29.

The application as amended is believed to be in condition for allowance and applicants hereby request the withdrawal of the rejection under 35 USC § 112, first paragraph and the rejection for obviousness double patenting and request passage of the application to issuance. The Commissioner is hereby authorized to charge any fees due for this submission to Deposit Account No. 50-0423, as well as credit any refunds.

Respectfully submitted,

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